**Output of the SARS-CoV-2 subgroup endorsed by ACDP**

# Biosafety Considerations for Deliberate Work Involving SARS-CoV-2; Change in HG classification.

## Target Audience

This document is aimed at anyone with an interest in the scientific reasoning for the change in the containment and control measures required for conducting deliberate work with SARS-CoV-2 in research, diagnostic or commercial facilities in Great Britain (GB) as agreed by the Advisory Committee on Dangerous Pathogens (ACDP); an expert committee providing independent scientific advice on the risks of exposure to various pathogens.

## Introduction

The hazard group (HG) for SARS-CoV-2 has been reduced from HG3 to HG2 in the 6th Edition of The Approved List of biological agents.

This document outlines the steps that were taken to reach that decision and considerations in how to manage potential future risks from any novel higher risk strains of SARS-CoV-2. It considers :

1. The review process for the hazard group (HG) re-classification of SARS-CoV-2,
2. The current scientific rationale for re-classification as HG2, and
3. The mechanisms to respond to potentially higher risk SARS-CoV-2 strains that could require classification as HG3.

This document does not apply to Genetically modified (GM) SARS-CoV-2. Assessment of GM activities with SARS-CoV-2 must be undertaken in line with The Genetically Modified Organisms (Contained Use) Regulations 2014.

## Background and Review

In July 2021, SARS-CoV-2 was added to the 4th Edition of the Approved List of Biological Agents as a HG3 biological agent. Classification as a HG3 biological agent requires deliberate work with the agent to be undertaken at Containment level (CL) 3 using defined CL3 control measures. Some non-propagative diagnostic work with the SARS-CoV-2 virus was permitted to be conducted at CL2 with additional precautions as identified through risk assessment. This was in line with recommendations by the World Health Organization (WHO) at that time.

As the pandemic progressed, knowledge increased significantly concerning scientific and clinical aspects of the virus and the disease it causes, population immunity, and the availability of medical interventions, in particular, safe and effective vaccines.

In March 2024, the WHO issued updated biosafety guidance, advising that most laboratory activities with SARS-CoV-2 could be safely undertaken at CL2, including activities previously considered as high-risk. Since then, Hong Kong is classifying any Omicron and descendent variants as equivalent of HG2 whilst prior variants remain HG3 and several countries (e.g., USA and Singapore) have moved or are moving to reclassify SARS-CoV-2 from HG3 to HG2 (or HG2 equivalent).

In 2025, ACDP's scientific, medical, and biosafety experts undertook a review of the current clinical and scientific knowledge of SARS-CoV-2, to re-evaluate the appropriateness of the current designation of SARS-CoV-2 as a HG3 agent. The outcome of this review recommended

that the HG for SARS-CoV-2 should be re-classified to HG2. ACDP also recommended that a SARS-CoV-2 working group should be convened to consider under what circumstances (e.g., new, significantly different strains), SARS-CoV-2 might present a higher risk, such that it should be classified as HG3 and subsequently handled at CL3.

The SARS-CoV-2 working group consisted of a diverse group of people representing the different relevant sectors working with the virus. This included individuals from academia, NHS medical consultants and infection specialists, the UK Health Security Agency (UKHSA), NERVTAG (New and Emerging Respiratory Virus Threats Advisory Group - GOV.UK), and the 'G2P-UK' National Virology Consortium, which studies how changes to the virus affect its behaviour and ability to cause disease.

The working group considered the available information on SARS-CoV-2 characteristics and population impact and produced this guidance note on 'Biosafety Considerations for Deliberate Work Involving SARS-CoV-2; Change in HG Classification'.

**Scientific rationale for reducing HG**

*Basis for HG classification*

Biological agents are classified according to the level of risk posed by the **deliberate manipulation** of the agent of infection to otherwise healthy individuals based on:

- The ability to cause infection;
- The severity of the disease that may result;
- How likely it is that the infection would spread to the community; and
- The availability of any prophylaxis or effective treatment.

A HG2 biological agent can cause human disease and may be a hazard to employees; it is unlikely to spread to the community and there is usually effective prophylaxis or treatment available.

A HG3 biological agent can cause severe human disease and may be a serious hazard to employees; it may spread to the community, but there is usually effective prophylaxis or treatment available.

In the definitions above, the ability of a pathogen to spread to the community takes into consideration those agents that are already endemic in a population. Infection resulting from deliberate activities with an agent, has a lower risk of causing an onward outbreak in a community if that agent is already circulating in the general population.

*Initial SARS-CoV-2 HG classification*

In the first year of the COVID-19 pandemic, individuals infected with SARS-CoV-2 presented more frequently with severe disease, there was evidence of community spread within the immunologically naïve population, and no vaccines or proven treatments were initially available. Thus, at the time, the definition of a HG3 biological agent was met. This was similar to other coronaviruses that can cause severe disease in humans (e.g., SARS-CoV-1, MERS-CoV).

*Reviewed SARS-CoV-2 HG classification*

Since the first year of the pandemic, the scientific and clinical knowledge of SARS-CoV-2 and available medical interventions have significantly increased, including the availability of vaccines

that prevent significant illness and pharmaceuticals to prevent and treat more severe illness in the most vulnerable risk groups.

The working group participated in a review of the currently available information on the disease it causes, population immunity, and the availability of medical interventions.

Over the past 5 years, a combination of vaccination and natural infection has given rise to increasing population partial immunity to SARS-CoV-2, such that there is protection from severe disease but not from re-infection and transmission. The office for national statistics (ONS) published figures in March 2023[1] indicating that 74% to 80% of adults across the UK, were estimated to have antibodies at a level indicating previous infection and/or vaccination.

Increased hybrid immunity (protection from a combination of both vaccination and infection) in the population is reflected in milder disease and significantly lower hospitalisation rates[2,3], as SARS-CoV-2 transitions from a pandemic to endemic virus. SARS-CoV-2 has shifted to a clinical burden profile similar to other regularly circulating respiratory viruses such as seasonal influenza virus. Prophylactic measures are available through NHS vaccination programmes for those most likely to have severe outcomes to infection and the NHS providing specific antiviral or monoclonal antibody treatment to individuals with COVID-19 who are at the highest risk of becoming seriously ill. In the event of severe inflammatory disease, several measures are available which improve the prognosis.

Collectively, SARS-CoV-2 now meets the definition of a HG2 agent.

*Likelihood of high-risk SARS-CoV-2 emerging*

Over time, changes in pathogens occur naturally. Whilst most of these changes do not increase pathogenicity, occasionally a biological agent with a higher virulence may emerge. Thus, the working group considered what changes in SARS-CoV-2 could affect virulence, with a focus on the potential for evasion from any of the many parts of the immune system, the severity of the COVID-19 disease, and the effectiveness of vaccines and treatments.

Genomic monitoring has identified hundreds of SARS-CoV-2 variants to date[4]. This sequencing effort has identified a spectrum of different viral spike proteins, (the main target for neutralising antibodies generated by vaccination) and other viral components (recognised by other parts of the human immune system such as T-cells)[5]. Despite these changes in the virus altering the efficiency with which some parts of the immune system might recognise the virus, there is good evidence that the combined immunological response to the virus is effective at preventing severe disease. The existing T-cell immunity resulting from natural population exposure to the virus since 2020 continues to offer protection against severe disease for most people[6]. In addition, the range of SARS-CoV-2 prophylactic vaccines and effective treatments continues to expand giving resilience to these arms of protection against severe disease outcomes[3].

Overall, it was considered by the working group, that currently the evidence pointed to a low likelihood of future SARS-CoV-2 variants causing a significant change in pathogenicity to warrant re-classification back from HG2 to HG3. It was noted however, that should mutations in the SARS-CoV-2 genome occur, which could lead to a significant change in viral virulence by increased viral transmission, altered tropism, evasion of established immunity and/or available prophylaxis and treatment, then consideration of whether it remained SARS-CoV-2 or had evolved into a new novel virus might be required, with subsequent analysis of the risk posed from this new novel variant or new virus undertaken.

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## Measures and pathways to respond to potentially higher risk SARS-CoV-2 strains or those which are significantly altered genetically, and may require re-classification as HG3

*Existing general mechanisms*

In the event of a significant new biological agent emerging or a new variant with altered tropism and requiring an urgent classification, ACDP will make provision for a review to enable an initial classification of the agent to be made. However, this would only be appropriate where the indications are that the initial classification will be HG3 or 4, and for which significant, urgent research is required by multiple users. In this eventuality, HSE will publish this classification.

More generally, HG classifications in The Approved List of biological agents are linked to a set of required containment and control measures for deliberate work with a biological agent. These are detailed in the Containment Tables in Schedule 3 of the Control of Substances Hazardous to Health Regulations (COSHH) 2002 (as amended). However, all laboratories should perform a comprehensive risk assessment to identify site and activity-specific risks associated with their work and to determine additional measures that might be required to mitigate these risks. Comprehensive risk assessments and mitigation measures are dependent on (but not limited to):

- The particular characteristics of the strain or variant used for deliberate work;
- The procedures performed, with certain procedures increasing the work's risk profile (e.g., aerosolization, animal work, large volumes, etc.);
- Identification of the hazards involved in the process and procedures;
- The competency level of the personnel who perform the procedures;
- The laboratory equipment and facility.

*SARS-CoV-2 specific considerations*

The working group acknowledges that due to the impact of the COVID-19 pandemic there is a need to identify any new SARS-CoV-2 variants that might present a higher risk and require classification as a HG3 agent.

Initial evidence for a significantly changed SARS-CoV-2 variant with increased virulence will most likely be observed within the healthcare sector due to increased cases, more severe disease and increased hospitalisations. The UK has a surveillance network that continuously monitors trends in infectious diseases through expert agencies, committees and groups. This includes:

- International epidemiological reports (e.g., through the New and Emerging Respiratory Virus Threats Advisory Group);
- Number of cases, syndromic and genomic surveillance (e.g. through UKHSA national flu and COVID-19 surveillance);
- Hospitalisation and ICU admission rates indicative of clinical severity of disease (e.g., through NHS data on COVID-19 Hospital Activity).

Additionally, researchers working with SARS-CoV-2 variants are required by the current Control of substances hazardous to health (COSHH) regulations 2002, (as amended)[7] to inform HSE if they identify any significant changes in the biological properties of the virus, which might alter the containment and control measures required to be implemented to mitigate the risks. This in turn would trigger an alert to ACDP for further consideration.

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Upon relevant reports, ACDP would review the available information, considering any available clinical and molecular signals that might be indicative of increased risk, and subsequently make an authoritative decision as to whether a HG3 classification is appropriate.

**SARS-CoV-2 working group membership**

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